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Applicant: Robert J. Peach, et al. **Examiner:** Not Yet Known
Serial No.: 09/865,321 **Group Art Unit:** 1646
Filed: May 23, 2001 **Docket No.:** 30436.57USU1
Title: SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF

CERTIFICATE UNDER 37 CFR 1.8:

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on March 6, 2002.


By: Tracy TruickSUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This Information Disclosure Statement is being filed herewith as a supplement to Applicant's June 19, 2001, Information Disclosure Statement which was submitted under 37 C.F.R. §1.97 (b)(1) within three months of the filing date of the national application (i.e. before August 23, 2001) on the merits. In accordance with 37 C.F.R. §1.98(d), copies of Exhibits 65-113 as set forth in the Form 1449 are included herewith.

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- Linsley, et al., 1991, *J.Exp.Med.* "CTLA-4 Is a Second Receptor for the B Cell Activation Antigen B7" 174:561-569. **(Exhibit 65)**
- Gimmi, et al., 1993, *Proc.Natl.Acad.Sci. USA* "Human T-Cell clonal anergy is induced by antigen presentation in the absence of B7 costimulation" 90:6586-6590. **(Exhibit 66)**
- Azuma et al., 1993 *Nature* "B70 antigen is a second ligand for CTLA-4 and CD28" 366:76-79. **(Exhibit 67)**
- Ronchese et al., 1994 *J.Exp.Med* "Mice Transgenic for a Soluble Form of Murine CTLA-4 Show Enhanced Expansion of Antigen-specific CD4 T Cells and Defective Antibody production In Vivo" 179:809-817. **(Exhibit 68)**
- Griggs et al., 1996 *J.Exp.Med* "The Relative Contribution of the CD28 and gp39 Costimulatory pathways in the Clonal Expansion and Pathgenic Acquisition of Self-reactive T Cells" 183:801-810. **(Exhibit 69)**
- Linsley et al., *J.Exp.Med* "CTLA-4 Is a Second Receptor for the B Cell Activation Antigen B7" 174:561-569. **(Exhibit 70)**
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- Tepper et al., 1994 *Transplantation Proceedings* "Tolerance Induction by soluble CTLA4 in a Mouse Skin Transplant Model" 26:3151-3154. **(Exhibit 77)**
- Perico et al., 1995 *Kidney International* "Toward novel antirejection strategies: In vivo immunosuppressive properties of CTLA4Ig" 47:241-246. **(Exhibit 78)**
- Finck et al., 1994 *Arthritis and Rheumatism* "Effects of CTLA4Ig in murine lupus" 37:S222. **(Exhibit 79)**
- Nishikawa et al., 1994 *Eur J. Immunol.* "Effect of CTLA-4 chimeric protein on rat autoimmune anti-glomerular basement membrane glomerulonephritis" 24:1249-1254. **(Exhibit 80)**
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- Webb, et al., 1996 *Eur J. Immunol* "Prevention and amelioration of collagen-induced arthritis by blockade of the CD28 co-stimulatory pathway: requirement for both B7-1 and B7-2," 26:2320-2328. **(Exhibit 84)**
- Van Oosterhout, et al., 1997 *Am.J.Respir. Cell Mol.Biol.* "Murine CTLA4-IgG Treatment Inhibits Airway Eosinophilia and Hyperresponsiveness and Attenuates IgE Upregulation in a Murine Model of allergic Asthma," 17:386-392. **(Exhibit 85)**
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- Spector, 1990 *Epidemiology of Rheumatic Disease* "Rheumatoid Arthritis," 16:513-537. **(Exhibit 96)**
- Liu MF, Kohsaka H Sakurai H, Azuma m Okumura K Saito I, Miyasaka N, 1996 *Arthritis-Rheum* "The presence of costimulatory molecules B7.1 (CD80) and B7.2 (CD86) in rheumatoid arthritis synovium". Jan; 39(1): 110-4. **(Exhibit 97)**

- Sfrikakis PP, Via CS. 1997 *Clin-Immunol-Immunopathol* "Expression of CD28, CTLA4, CD80, CD86 molecules in-patients with autoimmune rheumatic diseases: implications for immunotherapy". Jun; 83(3): 195-8. **(Exhibit 98)**
- Sayegh MH, Akalin E, Hancock WW, Russell ME, Carpenter CB, Linsley PS, Turka LA, 1995. *J. Exp. Med.* "CD28-B7 blockade after all antigenic challenge in vivo inhibits Th1 cytokines but spares Th2". 181: 1869-1874. **(Exhibit 99)**
- Racusen LC; et. al. 1999 *Kidney-Int.* "The Baniff 97 working classification of renal allograft pathology".. 55(2): 713- 723. **(Exhibit 100)**
- Parkin D, Jacoby A, McNamee P, 2000 *J Neurol Neurosurg Psychiatry* "Treatment of multiple sclerosis with interferon β : an appraisal of cost-effectiveness and quality of life"; 68: 144-149. **(Exhibit 101)**
- Nortvedt MW, Riise T, Myhr KM, and Nyland HI, 1999 *Neurology*. "Quality of life in multiple sclerosis: measuring the disease effects more broadly"; 53(5): 1098-1103 **(Exhibit 102)**
- Pearson TC, Alexander DZ, Winn KJ, Linsley PS, Lowry RP, Larsen CP, 1994 *Transplantation*. "Transplantation tolerance induced by CTLA4-Ig. 57:1701-1706. **(Exhibit 103)**
- Liao HX, Haynes BF, 1995 *Rheum-Dis-Clin-Noth-Am.* "Role of adhesion molecules in the pathogenesis of rheumatoid arthritis". Aug; 21(3): 715-40. **(Exhibit 104)**
- WO 95/33770, December 14, 1995, **(Exhibit 105)**
- Thomas R, Quinn C. 1996 *J-Immunol*. "Functional differentiation of dendritic cells in rheumatoid arthritis: role of CD86 in the synovium". Apr 15; 156(8): 3074-86. **(Exhibit 106)**

- Verhoeven-AC; Boers-M; Tugwell-P, 1998. "Combination therapy in rheumatoid arthritis: updated systematic review" *Br-J-Rheumatol.* Jun;37 (6): 612-619 (**Exhibit 107**)
- Schiff M, 1997 *Am-J-Med.* "Emerging treatments for rheumatoid arthritis". Jan 27; 102 (1A): 11S-15S (**Exhibit 108**)
- Balsa A, Dixey J, Sansom DM, Maddison PJ, Hall ND, 1996 *Br-J-Rheumato.* "Differential expression of the costimulatory molecules B7.1 (CD80) and B7.2 (CD86) in rheumatoid synovial tissue" *l.* Jan; 35(1): 33-7 (**Exhibit 109**)
- Ranheim Ea, Kipps Tj, 1994 *Arthritis-Rheum.* "Elevated expression of CD80 (B7/BB1) and other accessory molecules on synovial fluid mononuclear cell subsets in rheumatoid arthritis" Nov;37 (11): 1637-1647 (**Exhibit 110**)
- Freeman GJ, Gribben JG, Boussiotis VA, et. al. 1993 *Science.* "Cloning of B7-2: a CTLA-4 counter receptor that costimulates human T cell proliferation" 262: 909-911. (**Exhibit 111**)
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- Thomas R, Quinn C, 1996 *J-Immuno* "Functional differentiation of dendritic cells in rheumatoid arthritis: role of CD86 in the synovium" *l.* Apr 15;156(8): 3074-86 (**Exhibit 113**)

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,

Sarah B. Adriano

Sarah B. Adriano
Registration No. 34,470
Attorney for Applicants
Mandel & Adriano
35 No. Arroyo Parkway, Suite 60
Pasadena, California 91103
(626) 395-7801
Customer No. 26,941



FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary)	Docket Number 30436.57USU1	Application Number 09/865,321
	Applicant Robert J. Peach et al.	
	Filing Date May 23, 2001	Group Art Unit 1646

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLAS S	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLAS S	TRANSLATION	
						YES	NO
	WO 95/33770 (Exhibit 105)	December 14, 1995	PCT				X

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Linsley, et al., 1991, <i>J.Exp.Med.</i> "CTLA-4 Is a Second Receptor for the B Cell Activation Antigen B7" 174:561-569. (Exhibit 65)
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Filing Date

May 23, 2001

Group Art Unit

1646

(Use several sheets if necessary)

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

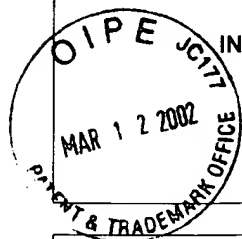
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*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



FORM 1449*

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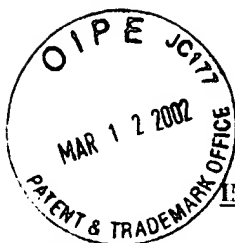
- Spector, 1990 *Epidemiology of Rheumatic Disease* "Rheumatoid Arthritis," 16:513-537. **(Exhibit 96)**
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CERTIFICATE UNDER 37 CFR 1.8

I hereby certify that this paper or fee is being deposited with the United States Postal as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on March 6, 2002.

By:

Name: Tracy Trick

35 N. Arroyo Parkway, Suite 60
Pasadena, California 91103
March 6, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.
- ☒ Supplemental Information Disclosure Statement (37 C.F.R. §1.97(b)(3))
- ☒ Form 1449 (Information Disclosure Statement)
- ☒ Exhibits 65 - 113
- ☒ Return postcard

Please charge any additional fees or credit overpayment to Deposit Account No. 50-0306. A duplicate of this sheet is enclosed.

MANDEL & ADRIANO

35 No. Arroyo Parkway, Suite 60
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